Remarks

It was noted in the Office Action (paper no. 11, page 1) that informalities were found on page 41 in which a portion of the table was illegible. Applicant has corrected these informalities by submitting a substitute paragraph. On page 41, the first and second lines in the footnote of the table, have been re-written in a legible form. No other changes were made to the text on page 41. Applicants have also amended the specification to correct the accidental deletion of a word at the bottom of Table 4 on page 28. No other changes were made to the text of page 28. No new matter is added by these corrections.

Rejection of Claims 36-46 Under 35 U.S.C. §112, first paragraph

Claims 42-58 have been rejected for lack of enablement under 35 U.S.C. §112, first paragraph. Applicant asserts that type of administration, times or frequencies of administration, and dosages required to obtain the desired effects are each addressed in the instant application. In the specification Applicants have provided support for each of these parameters. Applicants have described the type of administration, for example see page 54, lines 6-20. Applicants have described times or frequencies of administration, for example see page 53, lines 5-11, 19-25. Effective amounts and manner of determining effective amounts to obtain the desired effects are described in the specification, for example, page 54, line 21 through page 55, line 1. In addition, Applicant have provided a Declaration of Dr. Arthur Krieg describing experiments that have been performed and which demonstrate the ability of CpG oligonucleotides alone, or in combination with other compounds, to produce an immune response when delivered to a variety of different subjects, including human subjects, and by a variety of different modes. In addition, the Declaration describes data from human clinical trials. In view of the guidance and data presented in the specification, Applicants have met the necessary requirements to enable one of ordinary skill in the art to practice the invention.

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Accordingly, Applicants respectfully request that the Examiner withdraw the rejections made under 35 U.S.C. §112, first paragraph.

Summary

Applicants believe that each of the pending claims is in condition for allowance. Applicants respectfully request that the Examiner telephone the undersigned attorney in the event that the claims are not found to be in condition for allowance. If the Examiner has any questions and believes that a telephone conference with the applicants' attorney would prove helpful in expediting the prosecution of this application, the Examiner is urged to call the undersigned at the number listed below.

Respectfully Submitted,

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Docket No. C1039/7022(HCL/MXA)
July 23, 2001**X**
July 23, 2001

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Amended Paragraphs of the Specification

On page 28:

Table 4. secretion of Murine IL-6 induced by CpG DNA stimulation *in vivo*

Stimulant	IL-6 (pg/ml)
PBS	<50
E. coli DNA	13858±3143
Calf Thymus DNA	<50
CpG S-ODN	20715±606
non-CPG S-ODN	<50

Mice (2 mice/group) were i.v. injected with 100 µl of PBS, 200 µg of *E. coli* DNA or calf thymus DNA, or 500 µg of CpG S-ODN or non-CpG control S-ODN. Mice were bled 2 hr after injection and 1:10 dilution of each serum was analyzed of IL-6 ELISA. Sensitivity limit of IL-6 ELISA was 5 pg/ml. Sequences of the CpG S-ODN is 5'GCATGACGTTGAGCT3' (SEQ. ID. No: 6) and of the non-stimulatory S-ODN is 5'GCTAGATGTTAGCGT3' (SEQ. ID. NO: 4). Note that although there is a CpG in sequence 48, it is too close to the 3' end to effect stimulation, as explained herein. Data represent mean ±SD of duplicates. The experiment was done at least twice with similar results.

On page 41:

Table 13. Induction of human IL-12 secretion by Phosphorothioate CpG ODN

ODN	sequence (5'-3')	SEQ ID NO:	IL-12 (pg/ml) expt. 1	expt. 2
cells alone			0	0
1962	TCCTGTCGTTCCTTGTCGTT	52	19	0
1965	TCCTGTCGTTTTTTGTCGTT	53	36	0
1967	TCGTCGCTGTCTGCCCTTCTT	119	41	0
1968	TCGTCGCTGTTGTCGTTTCTT	120	24	0
2005	TCGTCGTTGTCGTTGTCGTT	47	25	0
2006	TCGTCGTTTTGTCGTTTTGTCGTT	46	29	15
2014	TGTCGTTGTCGTTGTCGTT	50	28	0
2015	TCGTCGTCGTCGTT	51	14	0
2016	TGTCGTTGTCGTT	85	3	0

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PBMC were collected from normal donors and spun over Ficoll, then cultured at 10^6 cells/well in 96 well microtiter plates with or without the indicated ODN which were added to cultures at 6 μg/ml. Supernatants were collected at 24 hr and tested for IL-12 levels by ELISA as described in methods. A standard curve was run in each experiment, which represents a different donor.

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